NANOTECHNOLOGY AND NANOMEDICINE-HEIGH–HO:THE AGE OF DWARFS

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ABSTRACT

It's a small wonder. Yes, nanotechnology is already touching our lives for better. The recent progress in the field of medicine has been phenomenal. None could have ever imagined that the Nanotechnology would have such a promising and extensive application in medical sciences. Right from developing newer therapeutics and imaging techniques to targeted drug delivery you can name it all. Nanotechnology science is still in its nascent stage with a long way to go. A nanometer is a billionth of a meter. Manipulation of matter on a very small scale is Nanotechnology and its utilization in medicine is Nanomedicine. In fact in recent times no other branch has seen the amalgation of such varied disciplines including physicists, chemists, engineers and biologists. Nanotechnology is still a very nascent science. It needs to grow and as its grows its true virtues and vices would come to fore.At the most now we can say that it has a very promising future. The genesis of nanotechnology can be traced to the promise of revolutionary advances across medicine, communications, genomics and robotics.

KEYWORDS: Nanotechnology, Nanoparticles, Nanomedicine, Smart drugs, Liposomes

INTRODUCTION

Nanotechnology in medicine is going to have a major impact on the survival of the human race.

Bernard Marcus

Nanotechnology is derived from Greek word **"NANO"** meaning Dwarf(Short Man). Nanomedicine involves utilization of nanotechnology for the benefit of human health and well being (1). Nanotechnology science is still in its nascent stage with a long way to go .A nanometer is a billionth of a meter. Manipulation of matter on a very small scale is Nanotechnology and its utilization in medicine is Nanomedicine. In fact in recent times no other branch has seen the amalgation of such varied disciplines including physicists, chemists, engineers and biologists. The most promising application of nanomaterials is the promise of targeted site specific drug delivery. The potential of eliminating tumorous outgrowth without any collateral damage through nanomaterials based drug delivery systems has created significant interest and the nanoparticles forms the basis for Bio-**nanomaterials** (2). Emergence of nanotechnology as a field in the 1980s occurred through convergence of Drexler's theoretical and public work, which developed and popularized a conceptual framework for nanotechnology, and high-visibility experimental advances that drew additional wide-scale attention to the prospects of atomic control of matter. In the 1980s, two major breakthroughs sparked the growth of nanotechnology in modern era. Working on a Nano scale is a challenging aspect of modern science. Over the past two decades, scientists and engineers have been trying to master the tits and bits of working with nanoscale materials. Now researchers have a clearer picture of how to create nanoscale materials with properties never envisioned before. Products using nanoscale materials and process are now available. Anti bacterial wound dressings use nanoscale silver. A nanoscale dry powder can neutralize gas. Batteries are being developed and matered with nanoscale materials in order to deliver more efficient power.

History Of Nanotechnology

The vision of nanotechnology introduced in 1959 by late Nobel Physicist Richard P Faynman in dinner talk said, "There is plenty of room at the bottom,"[3] proposed employing machine tools to make smaller machine tools, these are to be used in turn to make still smaller machine tools, and so on all the way down to the atomic level,

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noting that this is "a development which I think cannot be avoided". Infact his vision of Ultrasmall computers and various nanoscale microscale robots were way ahead of his times. Feynman's idea remained largely undiscussed until the mid-1980s, when the MIT educated engineer K Eric Drexler published "*Engines of Creation*", a book to popularize the potential of molecular nanotechnology (3).

The development in the field of nanotechnology started in 1958 and the various stages of development have been summarized in Table 1.

Year Development in nanotechnology

1959 R. Feynmaninitiatedthought process1974The term nanotechnology was used by Taniguchi for the first time.

1981 IBM Scanning Tunneling Microscope

1985 "Bucky Ball"

1986 First book on nanotechnology Engines of Creation published by K. Eric Drexler, Atomic Force Microscope

1989 IBM logo was made with individual atoms1991S. Iijima discovered Carbon Nano tube for the first time.

1999 1st nano medicine book by R. Freitas"Nano medicine" was published

2000 For the first time National Nanotechnology Initiative was launched

2001 For developing theory of nanometer-scale electronic devices and for synthesis and characterization of carbon nanotubes and nano wires, Feynman Prize in Nanotechnology was awarded

2002 Feynman Prize in Nanotechnology was awarded for using DNA to enable the self-assembly of new structures and for advancing our ability to model molecular machine systems.

2003 Feynman Prize in Nanotechnology was awarded for modeling the molecular and electronic structures of new materials and for integrating single molecule biological motors with nano-scale silicon devices.

2004 First policy conference on advanced nanotech was held. First center for nano mechanical systems was established, Feynman Prize in Nanotechnology was warded for designing stable protein structures and for constructing a novel enzyme with an altered function.

2005-2010 3D Nano systems like robotics, 3D networking and active nano products that change their state during use were prepared.

2011 Era of molecular nano technology started

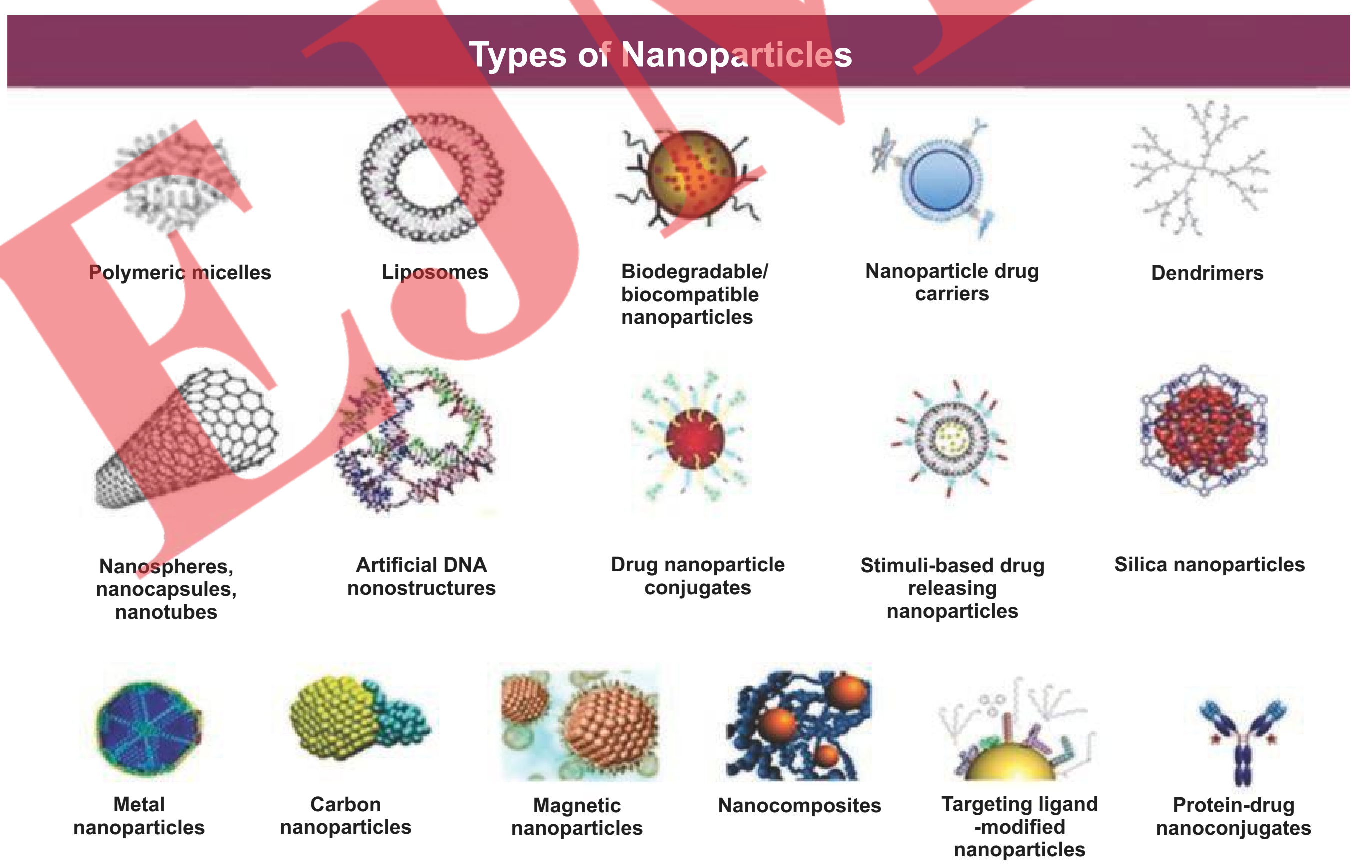

Fig 1. Torchilin, V (2006). "Multifunctional nanocarriers."Advanced Drug Delivery Reviews. 58 (14): 1532–55. doi:10.1016/j.addr.2006.09.009

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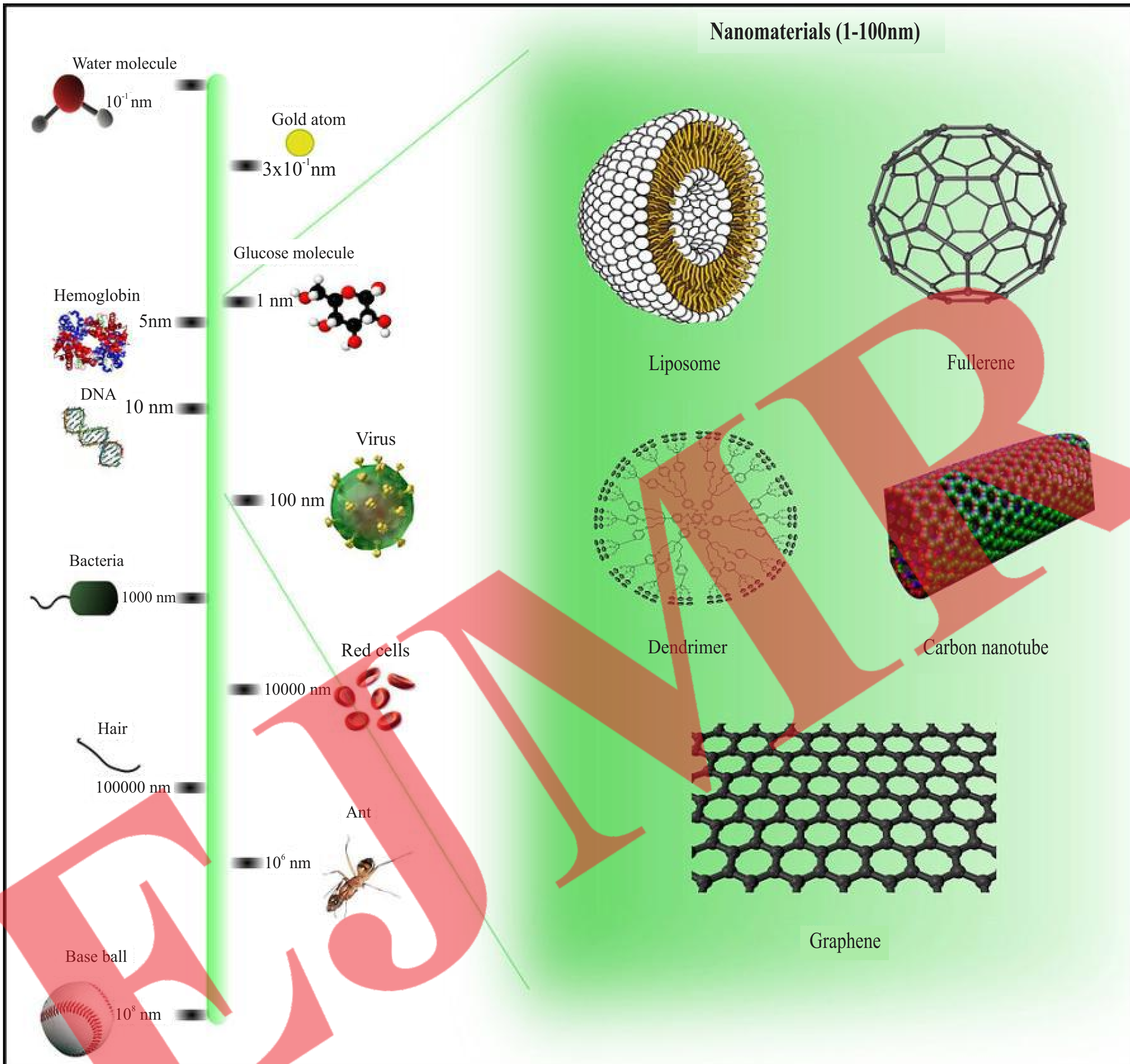

Fig.2.

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Nanodiagnostics

However Fancy the word Nanodiagnostics would seem, It is the use of nanodevices for the early disease identification or predisposition at cellular and molecular level. In *in-vitro* diagnostics, nanomedicine could increase the efficiency and reliability of the diagnostics using human fluids or tissues samples by using selective nanodevices, to make multiple analyses at subcellular scale, etc. In *in vivo* diagnostics, nanomedicine could develop devices able to work inside the human body in order to identify the early presence of a disease, to identify and quantify toxic molecules, tumor cells.

Nanoparticles In Medical Science

o Liposomes

o Quantum dots (Nanocrystals)

o Nanoshells

o Cantilevers- A Nanoelectromechanical Sensor (NEMS)

o Dendrimers

o Nanowires

Nanotechnology In Health And Medicine

Our world today is in a grip of Chronic inflammatory diseases. Inspite of good understanding of the web of causation of chronic diseases we still do have a no. of missing links. About 50 years back no one could have imagined the use of Nanomedicine to play a role in these diseases. Nano medicine is a relatively new field of science and technology.

By interacting with biological molecules at nano scale, nanotechnology broadens the field of research and application. Interactions of nano devices with bio molecules can be understood both in the extracellular medium and inside the human cells. Operation at nano scale allows exploitation of physical properties different from those observed at micro scale such as the volume/surface ratio. Programmable nanorobotic devices would allow physicians to perform precise interventions at the cellular and molecular level. Medical nanorobots have been proposed for genotological(4) applicatons in pharmaceuticals research, (5) clinical diagnosis, and in dentistry, (6) and also mechanically reversing atherosclerosis, improving respiratory capacity, enabling near-instantaneous homeostasis, supplementing immune system, rewriting or replacing DNA sequences in cells, repairing brain damage, and resolving gross cellular insults whether caused by irreversible process or by cryogenic storage of biological tissues.

Regenerative Medicine

In Greek mythology, Prometheus, meaning "forethought") is a Titan, Culture hero, and trickster figure who is credited with the creation of men from clay, and who defies the gods by stealing fire and giving it to humanity, an act that enabled progress and civilization. Prometheus is known for his intelligence and as a champion of mankind (7)

Fig 5.Prometheus depicted in a sculpture by Nicolas-Sebastien Adam, 1762 (Louvre).

The punishment of Prometheus as a consequence of the theft is a major theme of his mythology, and is a popular subject of both ancient and modern art. Zeus, king of the Olympian gods, sentenced the Titan to eternal torment for his transgression. The immortal Prometheus was bound to a rock, where each day an eagle, the emblem of Zeus, was sent to feed on his liver, which would then grow back overnight to be eaten again the next day. (In ancient Greece, the liver was often thought to be the seat of human emotions.

The human body is comprised of molecules, hence the availablity of molecular nanotechnology will permit dramatic progress to address medical problems and will use molecular knowledge to maintain and improve human health at the molecular scale. It is an emerging multidisciplinary field to look for the reparation, improvement, and maintenance of cells, tissues, and organs by applying cell therapy and tissue engineering methods. With the help of nanotechnology it is possible to interact with cell components, to manipulate the cell proliferation and differentiation, and the production and organization of extracellular matrices.

Present day nanomedicine exploits carefully structured nanoparticles such as dendrimers, carbon fullerenes (buckyballs), and nanoshells to target specific tissues and organs. These nanoparticles may serve as diagnostic and therapeutic antiviral, antitumor, or anticancer agents. Years ahead, complex nanodevices and even nanorobots will be fabricated, first of biological materials but later using more durable materials such as diamond to achieve the most powerful results. Magnetic nanoparticle capture presents an interesting and important utility to decontaminate biological products derived from potentially contaminated sources. Other methods, such as sodium hydroxide, sodium hypochlorite, and phosphotungstic acid treatments, destroy or remove prions but also damage the material of interest. In contrast, magnetic nanoparticles capture PrPSc with specificity (11). Recent progress in the field of nanotechnology has allowed corresponding rapid progress in regenerative medicine, particularly in biocompatible nanoscaffolds and tissue engineering.

Could we ever imagine complete reconstruction of damaged tissue, including the nervous system, bone, blood vessels, and potentially whole organs, by utilizing the tools and materials provided by nanotechnology in conjunction with stem cell therapy. This is just one more way in which nanotechnology is gradually transforming the world of medicine.

Cancer Therapy

According to the World Health Organization (WHO), there

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will be **15 million new cases of cancer worldwide in 2020**. More than 90% of cancer-related deaths occur by the spread of malignant cells to vital organs, a process called metastasis**.** Academia, Pharmaceutical and biotechnology companies are making substantial research investments in order to develop specific treatments that can destroy primary and secondary tumors, i.e. those resulting from metastasis to other organs.Very specific binding of the target molecules such as antibodies, small molecular weight ligands, or aptamers, attached to the surface of nanocarriers contribute to drug delivery to the tumors and this drug delivery is very efficient .However, the need of additional structures which are necessary for the stealth effect so as to exhibit selective tumor distribution along with the binding of targeting molecules for the targeting effect become the nanocarrier design in a highly challenging task. The three most studied types of nanoparticles for active targeting in cancer treatment are liposomes, lipid and polymerbased nanoparticles, and micelles. The advantage of actively (cancer cell) targeted nanomedicines over passively targeted formulations is that they are taken up by cancer cells much more efficiently, but it is necessary to remark that they need to penetrate several cell layers before being able to bind to cancer cells. Despite the significant progress that has been made with regard to better understanding the patho-physiological principles of drug targeting to tumors, several important pitfalls has been identified, such as insufficient incorporation of nanomedicine formulations in clinically relevant combination regimens. Another problem is that clinical practices require treatment for metastasis and not to solid tumor. It is well-known that patients with locally confined tumors can often be curatively treated with surgery and/or radiotherapy, and chemotherapy is only given in an adjuvant setting, to prevent and treat metastasis.

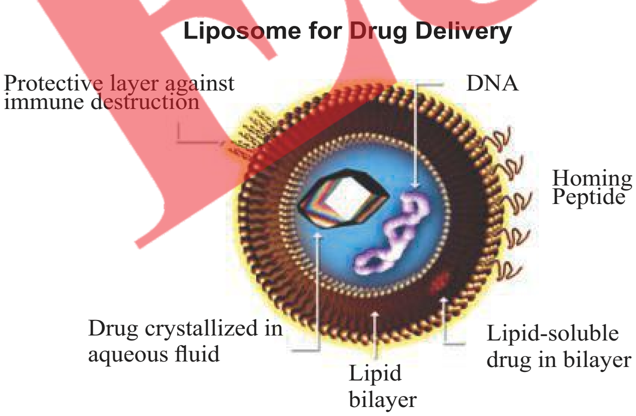

Fig 6. Liposome (1999) by Kosi Gramatikoff

Liposomes are composite structures made of phospholipids and may contain small amounts of other molecules. Though liposomes can vary in size from low micrometer range to tens of micrometers, unilamellar liposomes, as pictured here, are typically in the lower size range with various targeting ligands attached to their surface allowing for their surface-attachment and accumulation in pathological areas for treatment of disease.Nanomedicine has tremendous role in Cancer therapy it encompasses spectrum of effects right from imaging modalities to cancer therapeutics. Quantum dots when used in conjunction with magnetic resonance imaging, can produce exceptional images of tumor sites (8). These nanoparticles are much brighter than organic dyes and only need one light source for excitation which shows that the use of fluorescent quantum dots could produce a higher contrast image and at a lower cost than today's organic dyes used as contrast media. However a major point of concern is its toxicity.Future technologies may help in reducing the toxicities associated with use of Quantum dots. The most important property of nanoparticles in fact is high surface area to volume ratio, allows many functional groups to be attached to a nanoparticle, which can seek out and bind to certain tumor cells. Additionally, the small size of nanoparticles (10 to 100 nanometers), allows them to preferentially accumulate at tumor sites (because tumors lack an effective lymphatic drainage system).Sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers.One of the outstanding benefits of nanotechnology had been the use of this in imaging techniques and also in therapeutics.Nano particles probes now are doing a terrific job they can provide better visibility and enhanced signal intensity and better spatial resolution.The wonder of these nanoparticles are that these can serve to add radionucleide and fluorescent tags. For imaging modalities with low sensitivity, nanoparticles bearing multiple contrast groups provide signal amplification. The same nanoparticles can, in principle, deliver both the contrast medium and the drug, allowing monitoring of the bio-distribution and therapeutic activity simultaneously (referred to as theranostics) (9).

Iron oxide nanoparticles are one useful tool against cancer because, when "nano"-engineered with a specific coating, they bind particularly well to the tumors**.**Their magnetic properties make them suitable **imaging agents** with MRI-scans while their size and concentration in the tumor allow a **very high resolution and an accurate mapping of lesions**. Surgeons can thus rely on this to select properly patients and plan the surgical removal of the tumor**.**

Nanomedicine for cancer therapy and drug delivery

In therapy, nanotechnology is at the forefront of both targeted drug delivery and intrinsic therapies. For instance, nanoparticles can already be injected into the

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tumor and then be **activated to produce heat** and destroy cancer cells locally either by magnetic fields, X-Rays or light. Meanwhile the **encapsulation of existing chemotherapy drugs or genes** allows much more **localized delivery** both **reducing significantly the quantity of drugs absorbed by the patient for equal impact and the side effects on healthy tissues in the body**.

Coupling both modes of action has also been achieved with gold nanorods carrying chemotherapy drugs and locally excited in the tumor by infrared light. The induced heat both releases the encapsulated drug and helps destroying the cancer cells, resulting in a **combined effect of enhanced delivery and intrinsic therapy.**

Parkinson's disease

This can improve current therapy of Parkinson's disease (PD). Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease and affects one in every 100 persons above the age of 65 years, PD is a

disease of the central nervous system; neuro inflammatory responses are involved and leads to severe difficulties with body motions. The present day therapies aim to improve the functional capacity of the patient for as long as possible but cannot modify the progression of the neurodegenerative process.

Aim of applied nanotechnology is regeneration and neuro protection of the central nervous system (CNS) and will significantly benefit from basic nanotechnology research conducted in parallel with advances in neurophysiology, neuropathology and cell biology. The efforts are taken to develop novel technologies that directly or indirectly help in providing neuro protection and/or a permissive environment and active signaling cues for guided axon growth. In order to minimize the peripheral side-effects of conventional forms of Parkinson's disease therapy, research is focused on the design, biometric simulation and

optimization of an intracranial nano-enabled scaffold device (NESD) for the site-specific delivery of dopamine to the brain, as a strategy. Peptides and peptidic nano particles are newer tools for various CNS diseases.

Nanoparticles can be used for early imaging of neuronal loss and nanodevices can help in the detection/quantification of amyloid peptides in cerebrospinal fluid. Nanomaterials have been studied in experimental models of Parkinson's for the administration of antiparkinsonian agents, neurotrophic factors, antioxidants, neuroprotective and antiapoptotic factors. Nanotechnology-enabled naso-brain drug delivery, viral vectors, gene nanocarriers and exhaled breath analysis with nanoarray are other examples of nanotechnology applications. Scientists specialising in nanotechnology at Harvard University are pioneering the use of thin strands of miniscule mesh as a new alternative treatment for brain conditions such as Parkinson's disease.

Made of gold wires sandwiched between layers of a polymer, the mesh threads are small enough to fit in a syringe needle for injecting into the brain. Similar to deep brain stimulation (DBS) – a common electrical treatment for people with Parkinson's – the mesh is designed to deliver electric jolts to stimulate specific neurons and alleviate symptoms like tremors.

While DBS is more invasive, with its use of bulky electrodes that can disrupt the brain's neurons and cause scarring, the new tiny ribbons of mesh are far more discreet and spread out into a fishnet-like structure forming 'holes' which are large enough for neurons to pass through freely. This permeability to neurons mimics the flexibility of brain tissue and reduces scarring. The major challenges are also the difficulty of delivering of therapeutic agents to the major areas of brain.Transport of drugs are limited by the Blood Brain Barrier which is a major hurdle.A major strategy in the coming years is the use of technology to insert optimal amount of drugs via nanoparticles across blood brain barrier that could exhibit less peripheral side effects.

CONCLUSION

The new generation of nanoparticles might control the delivery of drugs both by prolonging drug circulation and by targeting the drug to the site of action in a specific manner. Further experiments are necessary to the better comprehension of the mechanisms which manage these different nanoparticle-mediated transport of the drugs to the brain, these nanoparticles may be helpful in the

treatment of brain diseases, because they offer clinical advantages such as decreased drug dose, reduced drug side effects, increased drug viability, non-invasive routes of administration, and improved patient quality of life.

Nanotechnology is still a very nascent science.It needs to grow and as its grows its true virtues and vices would come to fore.At the most now we can say that it has a very promising future. The genesis of nanotechnology can be traced to the promise of revolutionary advances across medicine, communications, genomics and robotics.

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